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Myoclonus Induced by the Use of Gabapentin

Myoclonus is a rare side effect of gabapentin (GBP) and has been reported in patients with preexisting myoclonus, mental retardation, chronic static encephalopathy, diffuse brain damage, impaired renal function, or end stage renal disease. We report a case of myoclonus in a patient with normal renal function and no previous disorders. A 69-year-old female underwent discectomy and foraminotomy at the left L4-L5 level. Postoperatively, she complained of paresthesia in her left leg, which was thought to be due to root manipulation during surgery. To relieve the paresthesia, she was given tramadol, an oral opioid agonist, and GBP. One week after GBP was increased to 900 mg per day, myoclonus developed, which severely impaired her normal activity. Her symptoms resolved 2 days after discontinuation of GBP. The coadministration of tramadol and GBP may mutually enhance the myoclonic potential of each drug. The causal relationship between GBP and myoclonus was suggested by cessation of myoclonus after GBP discontinuation despite continued therapy with tramadol.

KEY WORDS : Myoclonus · Gabapentin (GBP) · Opioids.

INTRODUCTION

Gabapentin (GBP) has anticonvulsant and analgesic properties. It is an effective medication in many disorders associated with chronic pain and neuropathic pain, in lumbar spinal stenosis, and in failed back surgery syndrome caused by epidural fibrosis^{3,7,15,16}. Although the evidence for the efficacy of GBP in acute pain is limited, preoperative oral GBP has been shown to be effective in reducing postoperative pain, including post-discectomy or post-fusion pain^{8,14}.

It is known that GBP has a favorable safety profile and few drug interactions^{2,4,7}. Nevertheless, a few studies have reported myoclonus associated with the use of GBP in patients with epilepsy, encephalopathy, impaired renal function, or end stage renal disease (ESRD)^{1,6,11,17}.

We present a case of myoclonus associated with the use of GBP in a 69-year-old female patient with normal renal function and no previous disorders.

CASE REPORT

A healthy 69-year-old woman underwent discectomy and foraminotomy at the L4-L5 level for the relief of left sciatic pain caused by stenosis with left-sided herniated disk at that level. Postoperatively, reduction of sciatic pain was noted, but patient complained of paresthesia in her left leg, possibly a result of root manipulation during surgery. To relieve the paresthesia, she was given tramadol without significant effect. We then added GBP, starting with 300 mg/day and increasing by 300 mg/day every 2 days up to 900 mg/day. After the addition of GBP, the paresthesia was much reduced.

One week after GBP was increased to 900mg/day, fast-frequency, high amplitude jerking and twitching of the head and four extremities developed, which severely impaired her normal activity. She could not drink or eat. Her mental status was normal and brain computed tomography, blood cell count, blood chemistry and urinalysis showed no abnormality. Her blood urea nitrogen was 10.2 mg/dl and creatinine was 0.8 mg/dl. GBP levels were not obtained. Continuous electroencephalography monitoring showed no cortical epileptiform discharges associated with the myoclonus. Her symptoms resolved two days after discontinuation of GBP.

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DISCUSSION

GBP may induce movement disorders at clinically recommended doses, and these disorders may develop within days of initiation and subside promptly after drug discontinuation^{6,11,12,17}. The incidence of myoclonus in 1486 patients with epilepsy taking GBP during premarketing studies was 0.1 %¹. However, Asconape et al. observed myoclonus in 12.5 % of 104 patients with epilepsy treated with GBP. In all cases, the myoclonus was subtle and did not significantly interfere with daily activities. The investigators suggested the risk factors for the development of myoclonus were preexisting myoclonus, mental retardation, chronic static encephalopathy, or diffuse brain damage¹.

It has also been reported that the incidence of GBP-related myoclonus in patients with impaired renal function or ESRD is relatively high^{6,17}. The reasons were as follows : (a) uremia can induce myoclonus; (b) GBP causes myoclonus through a mechanism different from that of uremia-induced myoclonus; and (c) GBP clearance is impaired in ESRD¹⁷. Furthermore, patients with ESRD have been reported to have more severe myoclonus and concomitant mental status changes following initiation or dosage-increase of GBP than that seen in the group described by Asconape et al., possibly because GBP exacerbates an encephalopathy^{6,17}.

The mechanisms of GBP-induced myoclonus remain poorly understood. It has been suggested that the serotonin neurotransmitter system may be involved, as this system has been intimately linked to myoclonus⁹. Whole blood levels of serotonin are increased in healthy volunteers receiving GBP¹⁰. However, GBP has not been shown to interact directly with serotonin receptors as an antagonist or agonist¹³.

In the present case, the patient had no encephalopathy or epilepsy and had grossly normal renal function. However, severe myoclonus that interfered with her daily activities developed without mental status change. The coadministration of tramadol and GBP might have mutually enhanced the myoclonic potential of each drug. In healthy volunteers, concomitant administration of morphine and GBP has been shown to enhance the acute analgesic effect of morphine and to cause increased plasma concentration of GBP^{5,12}. Although the serum level of GBP was not available in this patient, and the coadministration of opioid and GBP presented difficulties in explaining the cause of myoclonus, the causal relationship between GBP and

myoclonus was suggested by cessation of symptoms after GBP discontinuation despite continued therapy with tramadol.

CONCLUSION

Administration of GBP should be performed with caution in elderly patients or in patients with being treated with opioid, as well as in patients with preexisting myoclonus, mental retardation, chronic static encephalopathy, diffuse brain damage, or impaired renal function. Even in severe or disabling myoclonus, discontinuation of GBP can lead to symptom resolution.

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